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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO
10/699,597	10/30/2003	Ruxandra Draghia-Akli	AVSI-0027 (108328.00161)	7762
70225 7590 10001/2008 JACKSON WALKER LLP 901 MAIN STREET			EXAMINER	
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SUITE 6000 DALLAS, TX	75202		ART UNIT	PAPER NUMBER
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Application No. Applicant(s) 10/699 597 DRAGHIA-AKLI ET AL. Office Action Summary Examiner Art Unit MARIA B. MARVICH 1633 -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS. WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION. Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). Status 1) Responsive to communication(s) filed on 02 July 2008. 2a) ☐ This action is FINAL. 2b) This action is non-final. 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11, 453 O.G. 213. Disposition of Claims 4) Claim(s) 1-18 and 29-41 is/are pending in the application. 4a) Of the above claim(s) 6.9-18 and 29-38 is/are withdrawn from consideration. 5) Claim(s) _____ is/are allowed. 6) Claim(s) 1-5, 7, 8 and 39-41 is/are rejected. 7) Claim(s) _____ is/are objected to. 8) Claim(s) _____ are subject to restriction and/or election requirement. Application Papers 9) The specification is objected to by the Examiner. 10) ☐ The drawing(s) filed on 30 October 2003 is/are: a) ☐ accepted or b) ☐ objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a). Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d). 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152. Priority under 35 U.S.C. § 119 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f). a) All b) Some * c) None of: Certified copies of the priority documents have been received. 2. Certified copies of the priority documents have been received in Application No. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). * See the attached detailed Office action for a list of the certified copies not received. Attachment(s)

1) Notice of References Cited (PTO-892)

Notice of Draftsperson's Patent Drawing Review (PTO-948)
 Information Disclosure Statement(s) (PTO/SB/08)

Paper No(s)/Mail Date 2/17/04, 3/8/05 and 6/6/06.

Interview Summary (PTO-413)
 Paper No(s)/Mail Date.

6) Other:

Notice of Informal Patent Application

DETAILED ACTION

Claims 1-18 and 29-41 are pending in this office action.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1-8) in the reply filed on 7/2/08 is acknowledged. Applicants' arguments have been considered but have not been found persuasive. The methods of making and using the promoter have been demonstrated to be patentably distinct. As guidance, the MPEP teaches "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation of separate classification, or separate status in the art, or a different field of search as defined in MPEP § 808.02. That prima facie showing may be rebutted by appropriate showings or evidence by the applicant" (see MPEP 803). A search burden has been demonstrated for Groups I versus Group II and III as set forth in the restriction requirement. Briefly the Groups have been determined to have a separate classification and status in the art and as well to require distinct fields of search. Furthermore, in the event that the product is not patentable, a determination of whether each method of making and using the product is patentable over the art is based upon the particulars of the method and not on the product made by or used in the method. Conversely, a search of any given process of making or using the product does not adequately support patentability of the product because the product can be made by or used in a materially different process. Therefore, until the product is deemed allowable, search and examination of the process claims with the product imposes an undue burden on the Office. As discussed previously, if a product claim is found allowable, withdrawn process claims that

depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04.

As well, applicants elect with traverse SEQ ID NO:5 and SEQ ID NO:1. Applicants' arguments have been considered but are not persuasive. This decision is not based upon the similarity of classification of the sequences but rather Applicant is directed to the Pre-OG Notice published March 27 rescinding the 1996 OG Notice: Examination of Patent Applications. As set forth in this notice, the sequences will be examined for independence, relatedness, distinction and burden as for claims to any other type of molecule. MPEP 2434 is directed to examination of sequences and guidelines so established because of the enormous number of applications appearing in the office that comprise large numbers of nucleic acids. MPEP 2434 teaches, "Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct invention, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141." Furthermore, MPEP 803.04 states; Nucleotide sequences encoding different proteins are structurally distinct chemical compounds and are unrelated to one another. These sequences are thus deemed to normally constitutive independent and distinct inventions within the meaning of 35 U.S.C. 121. Absent evidence to the contrary, each such nucleotide sequence is presumed to represent an independent and distinct, subject to a restriction requirement pursuant to 35 U.S.C. 121 and 37 CFR 1.141 et seq. It has been determined that one sequence for each enzyme used in the above method constitutes a reasonable number for examination purposes under the present conditions. At present huge number of submissions of claims directed to various sequences or to the use of such large number of sequences, such as nucleic acids or polypeptides, is so large that the election of 1 (ONE) sequence for each type of

enzyme used in the claimed method is now deemed to be practically appropriate so as to not overwhelm the examination and search processes for such claims. Examination will be restricted to a method of using only one sequence for each type of enzyme.

However, upon reconsideration the sequence requirement of SEQ ID NO:1-4 has been dropped as these are subcombinations that make up each of SEQ ID NO:5 5 and 16-22. Newly added claim 41 is drawn to a series of vectors that appear to comprise SEQ ID NO:5 in operable linkage with GHRH. As far as these vectors read on comprising SEQ ID NO:5 they will be examined. However, should any of the vectors comprise a promoter other then SEQ ID NO:5 these will be withdrawn from consideration.

The requirement is still deemed proper and is therefore made FINAL. Claims 6, 9-18 and 29-41 are withdrawn from consideration as being drawn to nonelected inventions.

Information Disclosure Statement

IDS' filed 2/17/04, 3/8/05 and 6/6/06 have been identified and the documents considered. The signed and initialed PTO Form 1449 has been mailed with this action. In the IDS filed 6/6/06, the European Search Report has been considered but has been crossed off of the 1449 as it does not constitute a documents under 37 CFR 1.98.

Specification

The abstract of the disclosure is objected to because it exceeds 150 words. Correction is required. See MPEP § 608.01(b).

Sequence Compliance

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below or on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Specifically, pages figures 12-19 each comprise two sequences that are not identified by SEQ ID NO:. If the sequences can be found in the sequence listing it would be remedial to insert the appropriate SEQ ID NO:s. If not, a substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, CRF and letter stating that the contents of the sequence listing and the CRF are the same and contain no new matter is required. The nature of the non-compliance did not preclude the examination on the merits of the instant application, the results of which follow.

Claim Objections

Claim 39 is drawn to non-elected subject matter.

Claims 1-5, 7 and 8 are objected to because of the following informalities: for grammatical accuracy, the phrase in claim 1, line 3, "into a first-population of cells forming" should be amended to —into a first-population of cells to produce—.

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Claims 2 and 4 recite, for example, "cells comprise cells in vitro". The population does not comprise cells in vitro but, more accurately, the population of --cells are in vitro--. The same is true of recitation that the "cells comprises cells in vivo".

Claim 3 recites "further comprising: second-screening the first cardiac-specific-clone" which for grammatical clarity should be amended to --further comprising: a second-screening of the first cardiac-specific-promoter--. It is recommended throughout the claims that the word "clone" be amended to recite --promoter-- or _expression construct-- as clones typically refer to clonal cell lines.

Claim 5 requires the article "the "prior to cardiac specific synthetic promoter".

In claim 7, line 3, the word "being" is not necessary in the claim and should be deleted.

In line 3, an article is required prior to "library of randomized synthetic-promoter-recombinants".

In claim 8, the recitation "the cis-acting regulatory elements comprise" is grammatically incorrect as elements should be singular.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1, 3 and 7 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claim 1 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: in step (c), the claim recites "utilizing the cardiac specific-synthetic promoter form the first-cardiac-specific clones as the cardiac specific-synthetic promoter for a cardiac-specific -synthetic expression construct". First, in step (b) the clones are only screened but and lack a step such as, --wherein if the transcriptional activity of a cell from the first-test-population of cells is higher then the control transcriptional activity then the cell is a first-cardiac-specific clone--. Secondly, the promoter is "utilized" in step (c) but it is not clear how the promoter is to be utilized. In other words the promoter can be isolated from the clone and ligated to an expression construct or the clone can be used straight-away as the claim further states that the randomized promoter is part of an expression construct.

Claim 1 recites the limitation "the control-cardiac-specific-clone" in line 14. There is insufficient antecedent basis for this limitation in the claim.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: what is involved in "second screening the first cardiac-specific-clone".

As well, the claim recites that "the reporter gene from the first-cardiac-specific-clone having a second-transcriptional activity in the second population of cells that is higher than a second-control-transcriptional activity of the control-cardiac-specific-clone introduced into the second-population of cells". First, there are two "second-population of cells" and while each have the same name, they appear to be distinct cell populations. Hence, the antecedent basis is

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very unclear of each. As well, a reporter gene cannot have transcriptional activity. It is expressed but itself does not have activity.

Claim 7 recites the limitation "the expressible gene" in line 6. There is insufficient antecedent basis for this limitation in the claim.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP
§ 2172.01. The omitted steps are: how a first combination of cis-acting regulatory elements are selected from library of randomized synthetic-promoter-recombinants".

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 7, 8 and 39-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 1 is drawn to a genus of cardiac specific synthetic promoters that are produced by screening a library of randomized synthetic promoter recombinant expression constructs into a test cell and assaying the activity of the promoter as compared to a control. This is a "reach-

through" claim that requires possession of a compound identified through the claimed methods. The written description requirement under 35 USC 112, first paragraph may be met by sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus.

Applicant is referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov).

The written description requirement for genus claims may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with known or disclosed correlations between function and structure, or by a combination of such characteristics sufficient to show that the applicant was in possession of the claimed genus.

The specification teaches that cardiac and skeletal muscles are attractive targets for transfection, however, expression levels are attained that are typically too low and therefore the invention is directed at construction of synthetic promoters for such use. Applicants claim a genus of promoters obtained by a process of screening "randomized synthetic-promoter-recombinant expression constructs". The specification teaches that by randomized means that cis-acting elements that are present in the art are assembly randomly into synthetic promoter (see

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comprise SEQ ID NO:1, 2, 3 or 4 in operable linkage with one another. Eight recombinant promoters comprising a variety of these elements are disclosed as SEQ ID NO:5 and 16-22. However, claims 1-5, 7 and 8 are drawn to promoters that are to be obtained. In other words, applicants are not in possession of the genus of promoters recited in claims 1-5, 7 and 8. Rather applicants are in possession of a cardiac specific promoter comprising more then one cis-acting element selected from the group of SEQ ID NO:1-4 in operable linkage. Specifically, applicants are in possession of for example SEQ ID NO:5 which comprises these elements as set forth below.



While one of skill in the art can readily envision numerable species of nucleic acid sequences that are obtained by the instant method, the fact remains that the actual nucleic acid sequences which encode a protein with a particular activity cannot be envisioned any better when the possible choices are narrowed from all possible sequences to all possible sequences with an arbitrary structural relationship with a known functional sequence. "Possession may not be shown by merely describing how to obtain possession of members of the claimed genus or how to identify their common structural features." Ex parte Kubin, 83 USPQ2d 1410, 1417 (Bd. Pat. App. & Int. 2007) citing University of Rochester, 358 F.3d at 927, 69 USPQ2d at 1895. Vas-

Cath Inc. v. Mahurkar, 19USPO2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116). Rather, the specification is directed to a promoter that is produced by operable linkage of more then one cis-acting element. The court and the Board have repeatedly held (Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPO2d 1016 (CA FC, 1991); Fiers v. Revel, 25 USPO2d 1601 (CA FC 1993); Fiddes v. Baird, 30 USPO2d 1481 (BPAI 1993) and Regents of the Univ. Calif. v. Eli Lilly & Co., 43 USPQ2d 1398 (CA FC, 1997)) that an adequate written description of a nucleic acid requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it, irrespective of the complexity or simplicity of the method; what is required is a description of the nucleic acid itself. Claiming all DNA's that achieve a result without defining what means will do so is not in compliance with the description requirement. Rather, it is an attempt to preempt the future before it has arrived. In this case, applicants claim a genus of promoter that are not described in the specification.

Claims 39 and 40 are drawn to vectors comprising c5-12 (SEQ ID NO:5), which comprises a specific combination of TEF-1, MEF1, MEF2 and SRE as set forth above, and at least one cis-acting regulatory element selected from SEQ ID NO:1-4. Hence, claims 39 and 40 are drawn to a modification of SEQ ID NO:5 in which additional elements are added. But the specification does not disclose such a promoter. Furthermore, claim 41 cannot be dependent

from such promoters as each of the vectors only comprise unmodified SEQ ID NO:5. Hence, claims 39-41 are not supported by the disclosure and are impermissible NEW MATTER.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Schwartz et al (US 5.298.422; see entire document).

Schwartz et al teach a myogenic vector for expression of a sequence in myogenic tissue (cardiac tissue) using a cardiac specific synthetic promoter (see e.g. figure 8). Because the Office does not have the facilities for examining and comparing the applicant's product with the products of the prior art, the burden is on the applicant to show a novel or unobvious difference between the claimed products and the products of the prior art (e.g. that the products of the prior art do not possess the same material structural and functional characteristics of the claimed product). See in re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977). Absent evidence to the contrary, the promoter of Schwartz et al is believed to be indistinguishable from those of the instant invention. While the instant invention recites that the promoter is the product of introducing a library of promoters into test cells and screening the cells for promoter activity, the steps are designed to identify a cardiac specific promoter and are not believed to induce any specific alterations that would distinguish the promoter from those of Schwartz et al. The

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construct comprising the cardiac specific promoter is used to express a gene such as GHRH in a cell (see example 8) and as demonstrated in figure 8 and 9, the cardiac specific promoter is linked to a gene resulting in an expression construct

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior at are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 7 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Draghia-Akli et al (US 7,241,744; see entire document).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicants claim a cardiac specific promoter comprising SEQ ID NO:5 or SEQ ID NO:1.

Draghia-Akli et al teach a promoter comprising SEQ ID NO:1 and furthermore this promoter is 99.7% identical to SEQ ID NO:5. The difference between the two is the first nucleotide which is missing from 10/315907. However, according to the diagram of SEO ID

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NO:5, this nucleotide does not perform a critical function nor does it function in the capacity of the promoter. KSR forecloses the argument that a specific teaching, suggestion or motivation is required to support a finding of obviousness. See the recent Board decision Exparte Smith -- USPD2d--, slip op. at 20, (BD. Pat. App. & Interfer. June 25, 2007). As well, it is within the ordinary skill of the art to use available methodologies to isolate a variety of promoters with C-terminal or N-terminal sequences removed that do not affect the function of the promoter. One would have been motivated to do so in order as the ability to modify sequences by applying conventional methodologies. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

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RESULT 1
US-10-315-907C-16
; Sequence 16, Application US/10315907C
; Patent No. 7241744
; GENERAL INFORMATION:
; APPLICANT: Advisys
; TITLE OF INVENTION: PLASMID MEDIATED SUPPLEMENTATION FOR TREATING
CHRONICALLY ILL SUBJECTS
; FILE REFERENCE: 108328.00073 - AVSI-0007
; CURRENT APPLICATION NUMBER: US/10/315,907C
; CURRENT FILING DATE: 2002-12-10
; NUMBER OF SEQ ID NOS: 25
; SOFTWARE: PatentIn version 3.1
; SEO ID NO 16
  LENGTH: 4260
  TYPE: DNA
  ORGANISM: Artificial sequence
   FEATURE:
   OTHER INFORMATION: Sequence for the pSP-SEAP cDNA construct
; Patent No. 7241744
US-10-315-907C-16
                        99.7%; Score 334; DB 5; Length 4260;
 Ouerv Match
 Best Local Similarity 100.0%; Pred. No. 1.8e-83;
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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MARIA B. MARVICH whose telephone number is (571)272-0774. The examiner can normally be reached on M-F (7:00-4:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, PhD can be reached on (571)-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Maria B Marvich, PhD Primary Examiner Art Unit 1633

/Maria B Marvich, PhD/ Primary Examiner, Art Unit 1633